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CLINICAL PRACTICE

Death due to a rare posttraumatic complication: fat embolism

Cristina Podilă[1], Mihaela C. Şomlea[2], Bogdan A. Buhaş[3], Adrian S. Judea[4], Andreea A. Hleşcu[5], Nicolae Nicoară[4], Flavia Săndoiu[1], Paula Marian[6], Bianca Hanganu[5], Irina S. Manoilescu[5,7]

Abstract: *Fat embolism is a rare complication of high or medium intensity trauma. It is caused by the formation of fat particles in the territories of small terminal circulation, especially at pulmonary, tegumentary and cerebral levels. The mechanism underlying the fat embolism is described by several different theories in literature. In legal medicine, fat embolism raises many controversies upon the diagnostic certainty of the thanatogenerator mechanism leading to death. The occurrence of fat embolism syndrome followed by death must be properly explained so that the fatality can be adequately framed from a legal point of view. In this paper the authors present three cases in which victims of trauma died due to clinically undiagnosed fat embolism, the diagnosis being established only by postmortem histopathological examination. The authors underline the fact that the diagnosis of fat embolism syndrome, although it is a clinical one, it is often established only during autopsy.*

Keywords: *fat embolism, trauma, death, autopsy, diagnosis*

INTRODUCTION

Embolism represents the motion through circulatory blood flow of a material which is not present in blood in normal conditions and its subsequent lodging inside the blood vessels. In the case of fat embolism, the material carried through the blood is represented by fat particles that reach the level of microcirculation. Fat embolism syndrome represents the systemic manifestation of the fat particles being present inside the microcirculation.

Fat embolism was first described by Zenker in 1862 in the case of a railroad worker who died of crushing injuries. In 1873 Bergmann diagnosed fat embolism in a living patient who had suffered a fracture of the femoral bone [1, 2].

The causes of fat emboli formation are multiple, both traumatic and non-traumatic. The most frequent traumatic causes are: long bone fractures, orthopedic procedures, soft tissue trauma (fat tissue laceration), liposuction and mastectomy, neurosurgical interventions. Non-traumatic causes include: acute pancreatitis, extensive burns, diabetes, fatty liver due to diets rich in extrinsic fats and oils [2, 3]. Exceptionally, fat embolism has been observed in cases of hepatic steatosis (in alcoholics and diabetic patients with hepatic damage) due to the destruction of hepatocytes and subsequent release of fat particles [4, 5].

[1] Bihor County Forensic Service, Oradea, Bihor, Romania
[2] County Clinical Emergency Hospital Cluj-Napoca, Clinical Department of Dermatovenerology
[3] County Emergency Hospital of Oradea, Department of Urology, Oradea, Romania
[4] University of Oradea, Faculty of Medicine and Pharmacy, Department of Morphological Disciplines, Oradea, Romania
[5] Grigore T. Popa University of Medicine and Pharmacy of Iasi, Romania, Department of Legal Medicine
[6] University of Oradea, Faculty of Medicine and Pharmacy, Department of Medical Disciplines
[7] Institute of Legal Medicine of Iași, Romania

Corresponding author: Andreea A. Hleşcu
andreea.velnic@yahoo.com

Fat embolism occurs in 90% of patients who have suffered a trauma, but only 2-5% of them develop the fat embolism syndrome; particularly at risk are those with fractures of the long bones. It is difficult to estimate the duration of this syndrome because the symptoms are often subacute or masked by other symptoms of trauma [2, 3].

Post-mortem studies have shown a different but a very high incidence of fat embolism. Thus, a study by Behn C. et al. on 527 autopsies demonstrated the presence of fat embolism in 92 of these [6]. Another study conducted by Hiss et al. in 1996, on 53 victims of aggression followed by death, showed a high incidence of fat embolism. All the subjects studied were young, male, victims of aggressions, suffering severe trauma 24 hours before death. In thirty two cases the presence of fat embolism was observed in the main organs, with no other obvious cause of death. The authors of the study hypothesized that the source of fat embolism was the mechanical disintegration of the subcutaneous adipose tissue [7].

In cases of fat embolism there is a poor correlation between post-mortem and clinical findings. This discrepancy ultimately gave rise to the concept of "iceberg effect of fat embolism" [8- 12]. This justifies, as well as cases with a insufficiently outlined clinical picture for a particular pathology, or a clinical picture that cannot explain the occurrence of death, the importance of forensic autopsy and postmortem laboratory investigations (histopathological and toxicological) in order to establish the thanatogenerator mechanism and the causal link between trauma / illness and death, and ultimately the legal nature of the case, i.e. suicide, accident or homicide [13- 19].

MATERIALS AND METHODS

We present three cases of trauma in which the cause of death was the fat embolism syndrome. All the cases are characterized by a rapid clinical deterioration leading to death, so that a clinical diagnosis of fat embolism syndrome could not be established antemortem.

Case no. 1

Male, 72 years old, chronic alcohol consumer, with past medical history of left femoral fracture and right sided craniotomy, is admitted to hospital for head trauma. At the time of admission physical examination revealed multiple ecchymoses, pain at the pelvic level, lower limbs and abdomen. Clinical and paraclinical investigations established the following diagnosis: minor craniocerebral trauma, facial trauma, posttraumatic subarachnoid hemorrhage, dura mater hygroma, abdominal contusion, pelvic contusion.

Surgical intervention was performed to evacuate the dura mater hygroma 6 days after the admission. Evolution was initially favorable. On the 4th postoperative day, the patient developed a febrile syndrome. Laboratory analysis highlighted: elevated leucocyte count (13.390 of which 11.270 neutrofils); elevated serum amylase (225 U/L); lowered erythrocyte count (3.83 milion); hematocrit levels as low as 40.08 %; low thrombocytes count (137.700); increased level of the liver enzyme AST to 48 U/L; low creatinine serum levels (0.69 mg/dl) and reduced glomerular filtration rate to 85 mil/min/1.73 m2. The next day the patient suffered cardiorespiratory arrest that did not respond to resuscitation maneuvers, followed by death. The forensic autopsy was performed. The external examination of the body showed: multiple injuries denoting violence such as ecchymoses and abrasions; signs of medical treatment at the level of the skull, i.e. recent surgical incision and an old whitish scar. The internal examination showed: on the head, 2 craniotomy areas, one of them being recent, subarachnoid hemorrhage, areas of flaccid cerebral structure, small petechial hemorrhagic areas disseminated throughout the brain. The examination of the lungs showed: pulmonary stasis and edema, and areas of pulmonary condensation. Fragments of brain and lungs were harvested during autopsy and subsequently examined by optic microscopy using the Sudan III staining. The microscopic examination revealed fat emboli in the brain and lungs. Following the postmortem macroscopic and microscopic examination we established that the cause of death was the fat embolism syndrome.

Case no. 2

Male, 54 years old, was admitted to the hospital with the diagnosis of: head trauma (subarachnoid hemorrhage, fracture of the left temporal bone with extension to the mastoid bone), face trauma (fracture of right jaw, comminuted fracture of the nose) and chest trauma (left pneumothorax, multiple rib fractures).

The patient was hospitalized for 35 days, during which multiple pleurotomies and bronchoscopies were performed. Laboratory examinations showed: increased leucocyte count (25.170 of which 21.100 neutrofils); low red blood cell count (2.612 milions); low hematocrit (21.240 %); low hemoglobin level (7.793 g/dl); normal thrombocyte count; increased level of AST (103 U/L); increased serum creatinine (4.28 mg/dl); increased GGT levels (93 U/L) and reduced glomerular filtration rate (10.8 mil/min/1.73 m2). Clinical evolution was initially favorable. On day 34 after admission the patient developed a feverish syndrome. The next day he suddenly suffered cardiorespiratory arrest, followed by death. A forensic autopsy was performed. The external examination of the cadaver revealed bruises and signs of

recent medical treatment. The internal examination showed: linear head fracture, subdural hematoma under partial resorption, small petechial hemorrhagic areas in the brain, pulmonary edema, and areas of pulmonary condensation. Fragments of organs were harvested (brain, lung) and examined by optic microscopy using Sudan III staining. Following the macroscopic and microscopic examinations we concluded that the cause of death was the fat embolism syndrome.

Case no. 3

Male, 20 years old, victim of a traffic accident, was admitted to the hospital with the diagnosis of: polytrauma due to road traffic accident, major craniocerebral trauma with diffused cerebral edema, multiple rib fractures, fracture of the left iliac wing and left ischial bones, fracture of the left femoral neck, and type III A fracture of the femoral diafisis. Patient was admitted in the hospital for 7 days and underwent a surgical intervention for the femoral fracture. During the first days after the surgery the patient was hemodynamically stable. On day 4 the patient showed tachypnea, tachycardia, and fever and his clinical condition suddenly worsen. The laboratory examinations showed: low leucocyte count (1.56 of which 1.37 neutrofils); reduced numbers of erythrocytes (2.31 milions); low hematocrit (23.3%); low hemoglobin (6.77 g/dl); reduced number of thrombocytes (58.600/ mmc); increase in liver enzyme AST (272 U/L) and ALT (250 U/L); increased serum creatinine (2.43 mg/dl); increased serum urea (94.16 mg/dl) and reduction of glomerular filtration rate to 27.21 mil/min/1.73 m2. Death occurred on the same day. At autopsy, the external examination of the corpse revealed: multiple ecchymoses, abrasions, hematomas, signs of medical treatment. The internal examination showed: brain contusion; multiple rib fractures; pulmonary edema, pulmonary condensation areas, pulmonary infarction; fractures of the pelvis and of the left femor. The microscopic examination of the fragments of brain and lungs collected during the autopsy and stained with Sudan III showed fat embolism. Therefore, based on macroscopic autopsy findings and histo-pathological examination of the brain and lung fragments, we established that the cause of death was the fat embolism syndrome.

RESULTS

In all the three cases the victims suffered various trauma: in the first case the victim suffered soft tissues and head injuries, in the second case the victim suffered a polytrauma with multiple fractures and soft tissue injuries and in the third case the victim suffered craniocerebral trauma, soft tissue injuries and long bone fractures. Therefore, in all the cases, the etiological conditions for the fat embolism occurrence were met. However, in none of the cases the diagnosis was clinically established antemortem. The examination by optic microscopy of the fragments of brain and lungs collected during autopsy and stained with Sudan III showed in all the cases the fat microemboli in the form of orange globes disseminated throughout the fields examined microscopically (figures 1-4) and allowed the postmortem diagnosis of fat embolism. Therefore, in all three cases presented, the results of the histopathological examination of the fragments harvested from the brain and the lungs during the autopsy were essential for determining the cause of death.

Figure 1: Microscopic aspect of brain tissue Sudan III stain x 40 (ice exam)

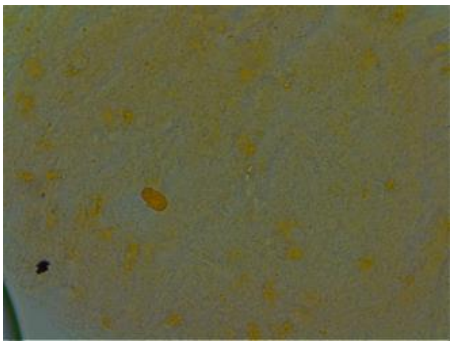


Figure 2: Microscopic aspect of lung tissue Sudan III stain x 20 (ice exam)

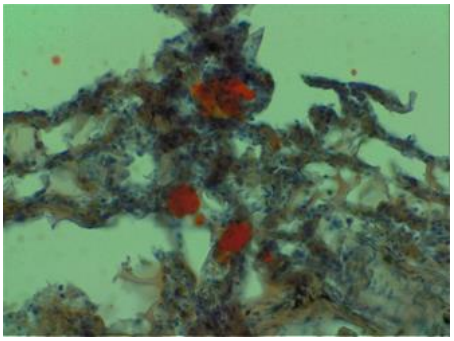


Figure 3: Microscopic aspect of lung tissue Sudan III stain x 40 (ice exam)

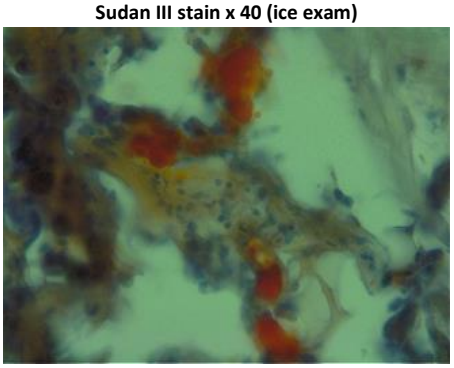
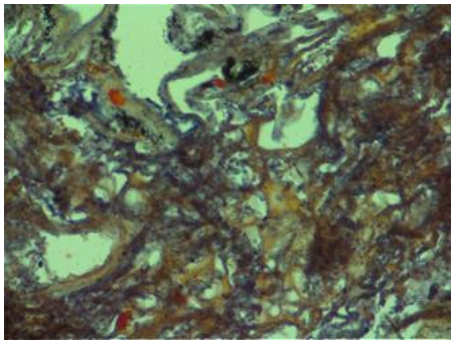


Figure 4: Microscopic aspect of lung tissue Sudan III stain x 10 (ice exam)



DISCUSSION

Fat embolism occurs due to the mobilization of fat cells or fat released by them, followed by their direct penetration into open blood vessels or lymphatic channels. Most emboli have a diameter of 15 to 40 μ; the fat emboli in the lungs are generally larger than those in the large arteries of the systemic circulation [11].

Several theories are mentioned in the literature to explain the pathogenesis of the fat embolism [20].

The mechanical theory shows that mobilization of fat particles occurs due to trauma to the bones or soft tissues. As a consequence, the fat particles released by the trauma enter the venous circulation from where they reach the lungs, where the majority remains, but some of them can also pass into the systemic circulation, reaching other organs.

The biochemical theory, also known as the emulsion instability theory, is mostly useful in explaining the non traumatic fat embolism.

The intravascular coagulation theory holds that in stressing conditions, substances that activate disseminated intra-vascular coagulation and aggregation of fat particles are released.

The toxic trauma theory claims that small blood vessels are affected by high concentrations of fatty acids in the plasma leading to increased vascular permeability.

The mechanical theory is based on the concept of the mobilization of fatty bone marrow from the long bones diaphysis. In the cases presented by us, only one patient suffered a recent fracture of the femur. In the other two cases we have to consider the trauma of soft tissues (hypodermic tissue) as the cause of the fat embolism, by noting that in both cases multiple ecchymoses were observed on the skin.

From a clinical point of view, Gurd and Wilson have developed the major and minor criteria which allow which allow for the diagnosis of fat embolism. The major criteria are: axillary or subconjunctival petechiae; hypoxaemia (PaO2 <60 mm Hg, FIO2 = 0); central nervous system depression disproportionate to hypoxaemia; pulmonary oedema; radiological signs and symptoms of respiratory insufficiency; cerebral changes unrelated to a cranial trauma or other illness; rash. The minor criteria are: tachycardia more than 110 bpm; pyrexia more than 38.5°C; fat globules present in urine; changes in renal function (reduced urine output); drop in haemoglobin level (more than 20% of the value upon admission); drop in haematocrit values; drop in platelet values (more than 50% of the value upon admission); increased erythrocyte sedimentation rate (greater than 71 mm per hour); fat globules present in the sputum; emboli present in the retina; tachicardia; fever; renal insufficiency; sudden thrombocytopenia. According to Gurd and Wilson the diagnosis of fat embolism can be established if either one major criterion and 4 minor criteria or 2 major criteria are met [21].

Lindeque suggested that the criteria of Gurd and Wilson may under-diagnose the syndrome, and proposed the following criteria based on respiratory parameters: Pao2 kPa of less than 8Fio2 0.21; Paco2 kPa or pH of less than 7.3 or more than 7.3; respiratory rate greater than 35 breaths/min−1 even after adequate sedation; increased breathing efforts showed by: dyspnea, use of accessory muscles, tachycardia and anxiety [22]. Any patient with a fractured femur and/or tibia, presenting one or more of these criteria, was diagnosed with fat embolism syndrome. These criteria led to the diagnosis of fat embolism syndrome in 29% of patients in a series of 55, which is higher than other series, especially since this study excludes patients with thoracic lesions, where some of Lindeque's clinical signs may appear in the absence of fat embolism [22].

Petechial eruption is considered a pathognomonic clinical sign for fat embolism syndrome. It may occur in about 60% of patients, usually on the conjunctiva, on the oral mucous membrane and on the skin of the neck and shoulders. This distribution can be explained by the drops of fat that accumulate in the aortic arch before the independent embolization at skin level through the subclavian and carotid vessels [20, 23-25]. The factors contributing to the petechial eruption are: stagnation of blood, loss of coagulation factors and platelets, and damage to the endothelial walls due to free fatty acids (FFA) leading to rupture of capillaries [25].

In the vast majority of cases, the fat embolism remains asymptomatic, and the fat emboli are dispersed into small cells and phagocyted by macrophages or embedded in

hepatic cells [26, 27]. Thus, many cases remain undiagnosed before death.

In the three cases presented, the symptomatology before death was poor and unspecific (febrile syndrome, tachycardia, tachypnea), and remained undiagnosed. The diagnosis of fat embolism syndrome was established only after performing the autopsy, and the histopathological examination of the brain and lung fragments stained specifically with Sudan III. Therefore, for post mortem diagnosis of fat embolism syndrome, it is essential to perform a histopathological examination with special stains that highlight the presence of fat emboli in the tissues and organs.

In the cases presented in this paper, fat embolism at the pulmonary and cerebral level was observed. According to literature, brain and lung localizations are the most important, although in most cases pulmonary fat embolism remains clinically asymptomatic. In order to be able to certify fat embolism as the cause of death, it is necessary for histopathological examinations to find fat emboli on a large part of the examination fields. The gravity of the consequences of pulmonary embolism also depends on the size and amount of fat emboli, as well as whether or not they pass into the systemic circulation to the lung.

In the brain, emboli produce small petechial hemorrhages, areas of ischemic necrosis and hemorrhage or necrosis and demyelination. Cerebral embolism is considered in literature as a paradoxical event, because it requires the presence of cardiac atrial septal defects in order to be explained. In the presented cases, there was no autopsy finding that showed neither atrial or ventricular septal defects nor patent arterial canal that could explain the cerebral fat embolism. An explanation of the pathophysiological mechanism which determined the cerebral embolism could not be found in this study.

The cause of death in all the three cases presented in this paper was the fat embolism. The diagnosis was established with certainty only after autopsy, by a histopathological examination which revealed the presence of fat emboli in the lung and brain tissues. Of the cases presented only one suffered a recent fracture of the femur; another presented in addition to trauma paraclinical changes suggestive of acute pancreatitis as a contributing factor; none had cardiac malformations that could explain the paradoxical fat embolism in the brain; all of the cases showed multiple lesions of the subcutaneous tissue and death occurred shortly after the initial trauma or after surgical interventions.

Death due to fat embolism can fall into the category of violent or non-violent deaths. Regardless of the cause of fat embolism, from forensic point of view the fat embolism is considered a complication that leads to a secondary causal relationship; in other words between the trauma/ initial pathology and death an intermediate link is inserted represented by a complication (the fat embolism) which is connected to a greater or lesser extent to the initial trauma/ pathology [28-30].

CONCLUSION

From forensic point of view, the diagnostic certainty in posttraumatic lesions is a priority objective. From the diagnosis it is possible to reconstruct the thanatogenerator mechanism and finally it can be useful to respond to the legal aspects of the case, i.e. the causal relationship between trauma and death.

In the case of trauma with reduced thanatogenerator potential, which usually evolve without complications, the occurrence of fat embolism syndrome followed by death must be appropriately explained so that the case can be properly framed from a legal point of view. It is important to emphasize that the histopathological examination using specific stainings, such as Sudan III, has a fundamental and incontestable role in the diagnosis of fat embolism and in estimating its gravity, and therefore, its implication in the occurence of death.

Conflict of interest: *The authors declare that there is no conflict of interest.*

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